SION RESUMED IN FILE 'USPAT' AT 16:41:38 ON 12 AUG 1997
FILE 'USPAT' ENTERED AT 16:41:38 ON 12 AUG 1997

=> d his

(FILE 'USPAT' ENTERED AT 16:34:29 ON 12 AUG 1997)

L1	198	S	424/529/CCLS
L2	111	S	424/533/CCLS
L3	85	S	424/534/CCLS
L4	338	S	L1 OR L2 OR L3
L5	17685	S	ANTIBIOTIC OR (BACTERIA# (5A) INHIBIT?)
L6	20	S	L4 AND L5
L7	14	S	424/93.73/CCLS
L8	55	S	424/93.71/CCLS
L9	64	S	L7 OR L8
L10	11	S	L9 AND L5

DT Conference
LA English

L1 ANSWER 32 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
AN 90:471924 BIOSIS
DN BA90:111344
TI THE ONTOGENY OF A 57-KD CATIONIC ANTIMICROBIAL PROTEIN OF HUMAN POLYMORPHONUCLEAR LEUKOCYTES LOCALIZATION TO A NOVEL GRANULE POPULATION.
AU PEREIRA H A; SPITZNAGEL J K; WINTON E F; SHAFER W M; MARTIN L E; GUZMAN G S; POHL J; SCOTT R W; MARRA M N; KINKADE J M JR
CS DEP. MICROBIOL. AND IMMUNOL., EMORY UNIV. SCH. MED., ROOM 3152, ROLLINS RES. CENT., ATLANTA, GA. 30322.
SO BLOOD 76 (4). 1990. 825-834. CODEN: BLOOAW ISSN: 0006-4971
LA English
AB The ontogeny of a 57-Kd cationic antimicrobial protein (CAP57) that has substantial similarities to bactericidal permeability increasing protein (BPI) has been determined immunocytochemically. CAP57 was detected in the granules of mature peripheral blood neutrophils. However, it was absent from other cells of the peripheral blood: eosinophils, red blood cells (RBCs), and mononuclear cells. In human bone marrow, CAP57 was confined to the neutrophilic series. The earliest stage of development of the myeloid cells at which CAP57 was demonstrated was the promyelocyte. Double immunofluorescent labeling showed that CAP57 was detected in cells positive for myeloperoxidase. The absence of lactoferrin in certain cells (promyelocytes) containing CAP57 indicated that CAP57 was synthesized and packaged in a population of granules prior to the development of granules that contain lactoferin. CAP57 could not be demonstrated in HL60 cells either by enzyme-linked immunosorbent assay (ELISA) or by immunocytochemistry. However, the presence of another granule-associated cationic antimicrobial protein of molecular weight 37 Kd (**CAP37**) was readily detected in undifferentiated HL60 cells. Amino acid sequence analysis showed that CAP57 and BPI were identical. Further indication of the identity between CAP57 and BPI was that monoclonal anti-CAP57 antibodies cross reacted with BPI. Sucrose density-gradient centrifugations showed CAP57 was confined to a granule population that exhibited a buoyant density intermediate of the previously described light and heavy azurophil granules. Further, resolution of the individual azurophil granule populations by Percoll density-gradient centrifugation revealed that CAP57 was most concentrated in the density range of 1.093 to 1.100 g/cc. These results strongly suggest the unique finding that CAP57 may be associated with a heretofore unreported granule type.

=> s bpi

L2 272 BPI

=> s antibiotic or antimicrobial

61397 ANTIBIOTIC
19576 ANTIMICROBIAL
L3 78303 ANTIBIOTIC OR ANTIMICROBIAL

=> s l2 and l3

L4 21 L2 AND L3

=> d ti 1-

L4 ANSWER 1 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI Crystal structure of human **BPI** and two bound phospholipids at 2.4 angstrom resolution.

non-phagocytic cells)
IT 103220-14-0, Defensin
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(defensins in granules of phagocytic and non-phagocytic cells)

L7 ANSWER 13 OF 27 CA COPYRIGHT 1997 ACS
AN 118:210811 CA
TI Antibiotic peptides and serine protease homologs in human polymorphonuclear leukocytes: Defensins and azurocidin
AU Gabay, Joelle E.; Almeida, Roque P.
CS Med. Coll., Cornell Univ., New York, NY, USA
SO Curr. Opin. Immunol. (1993), 5(1), 97-102
CODEN: COPIEL; ISSN: 0952-7915
DT Journal; **General Review**
LA English
AB A review, with 46 refs. The azurophil granule, a specialized lysosome of **neutrophils**, contains two families of **antimicrobial proteins**, each with four members. They are the defensins, comprising human **neutrophil protein** 1, -2, -3 and -4, on the one hand and the serprocidins, comprising cathepsin G, elastase, proteinase 3 and azurocidin, on the other. Defensins appear to contribute to mammalian as well as invertebrate immunity. Recent studies show that defensins and structurally related peptides are found not only in phagocytes but also in intestinal and respiratory cells. Aside from their antibiotic function, members of the defensin family may also act s hormonal agents. Within the serprocidin family the genes encoding the novel antibiotics and serine protease homologs azurocidin and proteinase 3 have been identified recently.
CC 15-0 (Immunochemistry)
ST review defensin azurocidin leukocyte
IT **Proteins**, specific or class
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(azurocidins, of human leukocytes)
IT Leukocyte
(polymorphonuclear, defensin and azurocidin of human)
IT 103220-14-0, Defensin
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(of human leukocytes)

L7 ANSWER 17 OF 27 CA COPYRIGHT 1997 ACS
AN 114:4444 CA
TI Antibiotic **proteins** of human **neutrophils**
AU Spitznagel, John K.
CS Sch. Med., Emory Univ., Atlanta, GA, 30322, USA
SO J. Clin. Invest. (1990), 86(5), 1381-6
CODEN: JCINAO; ISSN: 0021-9738
DT Journal; **General Review**
LA English
AB A review with 41 refs. **Proteins** described include defensins, cathepsin G and azurocidin and bactericidal/permeability increasing **protein**.
CC 15-0 (Immunochemistry)
ST review antibiotic **protein neutrophil**
IT **Neutrophil**
(**antimicrobial proteins** of human)
IT **Proteins**, specific or class
RL: BIOL (Biological study)
(BPI (bactericidal/permeability-increasing), as **neutrophil antimicrobial proteins**, of humans)
IT **Proteins**, specific or class

RL: BIOL (Biological study)
(azurocidins, as **neutrophil antimicrobial proteins**, of humans)
IT 56645-49-9, Cathepsin G 103220-14-0, Defensin
RL: BIOL (Biological study)
(as **neutrophil antimicrobial protein**, of humans)

L7 ANSWER 19 OF 27 CA COPYRIGHT 1997 ACS
AN 109:188318 CA
TI Human **neutrophil antimicrobial** activity
AU Thomas, Edwin L.; Lehrer, Robert I.
CS Dep. Biochem., St. Jude Child. Res. Hosp., Memphis, TN, USA
SO Rev. Infect. Dis. (1988), 10(Suppl. 2), S450-S456
CODEN: RINDDG; ISSN: 0162-0886
DT Journal; **General Review**
LA English
AB A review with 50 refs. O-dependent and -independent mechanism of **antimicrobial** action are discussed, including interactions with phagolysosomes, the bactericidal/permeability-increasing **protein**, cathepsin G, and the defensins.
CC 15-0 (Immunochemistry)
ST **neutrophil** biochem **antimicrobial** activity review
IT **Neutrophil**
(**antimicrobial** action of human, factors in)
IT Microbicidal and microbiostatic action
(of **neutrophil** of human, factors in)
IT **Proteins**, specific or class
RL: BIOL (Biological study)
(BPI, in **neutrophil antimicrobial** action, of human)
IT Lysosome
(phago-, in **neutrophil antimicrobial** action, of human)
IT 56645-49-9, Cathepsin G 103220-14-0, Defensin
RL: BIOL (Biological study)
(in **neutrophil antimicrobial** action of human)

L7 ANSWER 20 OF 27 CA COPYRIGHT 1997 ACS
AN 107:196014 CA
TI Lysosomal **proteins** of **neutrophils** as the factors of **antimicrobial** defense of cells
AU Lyzlova, S. N.
CS Leningr. State Univ., Leningrad, USSR
SO Vopr. Med. Khim. (1987), 33(5), 43-8
CODEN: VMDKAM; ISSN: 0042-8809
DT Journal; **General Review**
LA Russian
AB A review with 43 refs. discussing properties and functions of myeloperoxidase and other cationic **proteins** of **neutrophil** lysosome and interactions between various **antimicrobial** factors during phagocytosis. Inhibition of the O reactive species by **blood** serum **proteins** is considered.
CC 15-0 (Immunochemistry)
ST **neutrophil** lysosome **protein** **antimicrobial** review
IT Phagocytosis
(by **neutrophil**, lysosomal **proteins** in)
IT **Proteins**, biological studies
RL: BIOL (Biological study)
(lysosomal, in **neutrophil** microbicidal activity)
IT **Neutrophil**
(microbicidal action of and phagocytosis by, lysosomal **proteins** in)

IT Microbicidal and microbiostatic action
(of **neutrophil** lysosomal **proteins** in)
IT Lysosome
(**proteins** of, in **neutrophil** microbicidal activity)

L7 ANSWER 21 OF 27 CA COPYRIGHT 1997 ACS
AN 100:189850 CA
TI Complement-activating **antimicrobial proteins** (camp) of **blood** serum
AU Kawakami, Masanari
CS Med. Sch., Kitasato Univ., Sagamihara, Japan
SO Nippon Saikingaku Zasshi (1984), 39(1), 1-14
CODEN: NSKZAM; ISSN: 0021-4930
DT Journal; **General Review**
LA Japanese
AB A review with 48 refs. of the title **proteins** with respect to their types, physicochem. and immunol. properties, structure, specificity, and distribution in various animals.
CC 15-0 (Immunochemistry)
Section cross-reference(s): 10
ST review complement activator **antimicrobial** serum; **protein** complement activating serum review
IT Complement
RL: BIOL (Biological study)
(activation of, **antimicrobial proteins** of **blood** serum induction of)
IT **Proteins**
RL: BIOL (Biological study)
(complement-activating **antimicrobial**, of **blood** serum)
IT Microorganism
(inhibition of, complement-activating **proteins** of **blood** serum in)

=> d his

(FILE 'CA' ENTERED AT 10:34:06 ON 13 AUG 1997)
DELETE HIS
ACTIVATE A/A

L1 (710961) SEA FILE=CA BLOOD OR LEUCOCYTE# LEUKOCYTE# OR ERYTHROCYTE
L2 (991996) SEA FILE=CA PROTEIN#
L3 (25522) SEA FILE=CA ANTIMICROBIAL
L4 339 SEA FILE=CA L3 AND L1 AND L2

ACTIVATE B/A

L5 32952 SEA FILE=CA REVIEW/TI

L6 1179174 S REVIEW/DT
L7 27 S L6 AND L4

L4 ANSWER 2 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI Antineutrophil cytoplasm autoantibodies against bactericidal-permeability-increasing protein in inflammatory bowel disease.

L4 ANSWER 3 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI P15s (15-kD **antimicrobial** proteins) are stored in the secondary granules of rabbit granulocytes: Implications for antibacterial synergy with the bactericidal-permeability-increasing protein in inflammatory fluids.

L4 ANSWER 4 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI PhoP-PhoQ activates transcription of pmrAB, encoding a two-component regulatory system involved in Salmonella typhimurium **antimicrobial** peptide resistance.

L4 ANSWER 5 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI **Antibiotic** induced bacterial killing activates vascular endothelial cells and whole blood cells: Role of free lipopolysaccharide and soluble CD14.

L4 ANSWER 6 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI Frequency of anti-bactericidal-permeability-increasing protein (**BPI**) and anti-azurocidin in patients with renal disease.

L4 ANSWER 7 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI Time-resolved fluoroimmunoassay for bactericidal-permeability-increasing protein.

L4 ANSWER 8 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI Synergistic effect of a recombinant N-terminal fragment of bactericidal-permeability-increasing protein and cefamandole in treatment of rabbit gram-negative sepsis.

L4 ANSWER 9 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI Activity of synthetic peptides derived from bactericidal-permeability-increasing protein (**BPI**) on **antibiotic** resistant microbes.

L4 ANSWER 10 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI Salmonella typhimurium responses to a bactericidal protein from human neutrophils.

L4 ANSWER 11 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI A study of the interaction between recombinant bactericidal permeability increasing protein (rBPI-23) and gentamicin.

L4 ANSWER 12 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI Antibacterial proteins of granulocytes differ in interaction with endotoxin: Comparison of bactericidal-permeability-increasing protein, p15s, and defensins.

L4 ANSWER 13 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI Bactericidal-permeability-increasing protein (**BPI**) is an important antigen for anti-neutrophil cytoplasmic autoantibodies (ANCA) in vasculitis.

L4 ANSWER 14 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI Interactions between bactericidal-permeability increasing protein (**BPI**) and gentamicin.

L4 ANSWER 15 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI The region around residue 115 of human bactericidal-permeability increasing protein is not involved in lipopolysaccharide binding or bactericidal activity: Chemical synthesis and expression of a gene

coding for the active domain and characterization of recombinant proteins.

L4 ANSWER 16 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI ISOLATION OF TWO ISOFORMS OF A NOVEL 15-KDA PROTEIN FROM RABBIT POLYMORPHONUCLEAR LEUKOCYTES THAT MODULATE THE ANTIBACTERIAL ACTIONS OF OTHER LEUKOCYTE PROTEINS.

L4 ANSWER 17 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI THE ONTOGENY OF A 57-KD CATIONIC **ANTIMICROBIAL** PROTEIN OF HUMAN POLYMORPHONUCLEAR LEUKOCYTES LOCALIZATION TO A NOVEL GRANULE POPULATION.

L4 ANSWER 18 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI BACTERICIDAL-PERMEABILITY-INCREASING PROTEIN HAS ENDOTOXIN-NEUTRALIZING ACTIVITY.

L4 ANSWER 19 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI CLONING OF THE COMPLEMENTARY DNA OF A HUMAN NEUTROPHIL BACTERICIDAL PROTEIN STRUCTURAL AND FUNCTIONAL CORRELATIONS.

L4 ANSWER 20 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI EFFECTS OF THE BACTERICIDAL-PERMEABILITY-INCREASING PROTEIN OF POLYMORPHONUCLEAR LEUKOCYTES ON ISOLATED BACTERIAL CYTOPLASMIC MEMBRANE VESICLES.

L4 ANSWER 21 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
TI ROLE OF CHARGE AND HYDROPHOBIC INTERACTIONS IN THE ACTION OF THE BACTERICIDAL PERMEABILITY INCREASING PROTEIN OF NEUTROPHILS ON GRAM NEGATIVE BACTERIA.

=> d bib ab 3 12 18 21

L4 ANSWER 3 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
AN 97:82640 BIOSIS
DN 99374353
TI P15s (15-kD **antimicrobial** proteins) are stored in the secondary granules of rabbit granulocytes: Implications for antibacterial synergy with the bactericidal-permeability-increasing protein in inflammatory fluids.
AU Zarember K; Elsbach P; Shin-Kim K; Weiss J
CS Dep. Med., New York Univ. Sch. Med., 550 First Ave., New York, NY 10016, USA
SO Blood 89 (2). 1997. 672-679. ISSN: 0006-4971
LA English
AB The bactericidal potency toward complement-resistant Escherichia coli of bactericidal/permeability-increasing protein (**BPI**) released from polymorphonuclear leukocytes (PMNs) in glycogen-induced inflammatory peritoneal exudates of rabbits is dependent on synergy with extracellular p15s. This synergy depends an the high molar ratio of p15s to **BPI** in the extracellular fluid (apprx 50:1), which greatly exceeds the intracellular ratio (apprx 5:1). To explore the possible basis of the greater accumulation of p15s in inflammatory fluid, we examined the subcellular localization of **BPI** and p15 in PMNs. Immunogold electron microscopy confirmed the storage of **BPI** in primary granules and showed that p15s are stored in secondary granules. Reverse-transcription polymerase chain reaction of density-fractionated rabbit bone marrow cells verified that p15s are expressed later than **BPI** during myeloid differentiation. As the inflammatory response evolves, p15 mRNA appears earlier in blood and exudate cells than mRNA for **BPI**, consistent with release of progressively less mature precursors from bone marrow. Finally, Ca-2+-ionophore-mediated exocytosis of p15s occurs more readily than release of **BPI**.

We therefore propose that localization of a synergistic partner of **BPI** (p15s) in more readily released secondary granules allows the neutrophil to mobilize potent **BPI**-dependent antibacterial activity extracellularly without significant depletion of intracellular **BPI** stores.

L4 ANSWER 12 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
AN 95:307471 BIOSIS
DN 98321771
TI Antibacterial proteins of granulocytes differ in interaction with endotoxin: Comparison of bactericidal-permeability-increasing protein, p15s, and defensins.
AU Levy O; Ooi C E; Elsbach P; Doerfler M E; Lehrer R I; Weiss J
CS Dep. Microbiol., New York Unv. Sch. Medicine, 530 First Ave., New York, NY 10016, USA
SO Journal of Immunology 154 (10). 1995. 5403-5410. ISSN: 0022-1767
LA English
AB Bactericidal/permeability-increasing protein (**BPI**), antibacterial 15-kDa protein isoforms (p15s), and defensins (neutrophil peptides or NPs) are granule-associated antibacterial proteins of polymorphonuclear leukocytes (PMN) that have both direct and synergistic growth inhibitory activity against Gram-negative bacteria. In this study, we have compared in vitro the abilities of these antibacterial proteins, alone and in combination, to inhibit the endotoxic activity of isolated LPS and whole bacteria. All three proteins blocked endotoxic activity in: 1) the Limulus amoebocyte lysate assay, 2) priming of PMN for enhanced arachidonate release, and 3) stimulating leukocyte oxidase activity in 1 % blood. However, the proteins differ markedly in both relative potency (**BPI** mchgt p15s = NP1) in the presence of the plasma LPS-binding protein and in the range of LPS chemotypes that can be inhibited. **BPI** potently neutralizes LPS of any chemotype, but p15s and defensins are less active against long-chain (S-type) LPS. In whole blood ex vivo, the p15s and NP1 are approximately 1000-fold less potent than **BPI**, but at subinhibitory doses act in synergy with **BPI** to inhibit the TNF-inducing activity of a serum-resistant encapsulated strain of Escherichia coli (K1/r). The anti-endotoxic effects of p15 and NP1 against E. coli K1/r in whole blood appear secondary to growth arrest, because, in marked contrast to **BPI**, they are not evident against nonviable bacteria (pretreated with **antibiotic**) nor isolated LPS. Thus, **BPI** stands out for its ability to inhibit isolated or bacterial LPS under physiologic conditions. However, p15s and defensins may also contribute to suppression of endotoxic signaling by Gram-negative bacteria via synergistic (with **BPI**) growth inhibition upon extracellular release of these proteins from PMN during inflammation.

L4 ANSWER 18 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
AN 90:132197 BIOSIS
DN BA89:71008
TI BACTERICIDAL-PERMEABILITY-INCREASING PROTEIN HAS ENDOTOXIN-NEUTRALIZING ACTIVITY.
AU MARRA M N; WILDE C G; GRIFFITH J E; SNABLE J L; SCOTT R W
CS INVITRON CORP., 301 PENOSBSCOT DRIVER, REDWOOD CITY, CALIF. 94063.
SO J IMMUNOL 144 (2). 1990. 662-666. CODEN: JOIMA3 ISSN: 0022-1767
LA English
AB Neutrophil granules contain proteins important in host defense against bacterial pathogens. Granule proteins released from activated neutrophils facilitate opsonization, phagocytosis, tissue digestion, and **antimicrobial** activity. Three similar, if not identical, neutrophil proteins, bactericidal/permeability-increasing protein (**BPI**), 57,000 m.w. cationic **antimicrobial** protein, and bactericidal protein have been described that specifically kill gram negative bacteria. Since LPS is a structure

common to all gram-negative bacteria, we investigated whether the microbicidal protein **BPI** affects biologic activity of LPS in vitro. Human neutrophils can be activated both in vitro and in vivo by LPS. Upon stimulation, surface expression of CR1 and CR3 increases markedly. Using flow microfluorimetry, we analyzed surface expression of CR1 and CR3 as a measure of neutrophil stimulation in response to LPS. CR upregulation on neutrophils was TNF independent, suggesting direct LPS stimulation of neutrophils in this system. Purified **BPI** completely inhibited CR up-regulation on neutrophils stimulated with both rough and smooth LPS chemotypes at 1.8 to 3.6 nM (100 to 200 ng/ml). By comparison, the polypeptide **antibiotic** polymyxin B completely inhibited the same dose of LPS at 0.4 nM. The inhibitory activiy of **BPI** appeared to be specific for LPS because neutrophil stimulation by formylated peptide or TNF was unaffected. The specificity of **BPI** for LPS was further demonstrated by inhibition of LPS activity in the limulus amebocyte lysate assay. Therefore, the role of **BPI** in infection may not be limited to its microbicidal activity, but it may also regulate the neutrophil response to LPS.

L4 ANSWER 21 OF 21 BIOSIS COPYRIGHT 1997 BIOSIS
AN 84:194468 BIOSIS
DN BA77:27452
TI ROLE OF CHARGE AND HYDROPHOBIC INTERACTIONS IN THE ACTION OF THE BACTERICIDAL PERMEABILITY INCREASING PROTEIN OF NEUTROPHILS ON GRAM NEGATIVE BACTERIA.
AU WEISS J; VICTOR M; ELSBACH P
CS DEP. MED., NEW YORK UNIV. SCH. MED., N.Y. 10016.
SO J CLIN INVEST 71 (3). 1983. 540-549. CODEN: JCINAO ISSN: 0021-9738
LA English
AB Evidently, the action of purified cationic bactericidal-permeability-increasing protein (**BPI**) from neutrophils on susceptible gram-negative bacteria requires saturation binding to negatively charged surface sites. This charge interaction is necessary but not sufficient to produce the effects of [rabbit] **BPI** on the envelope and on viability. By altering the hydrophobic properties of the bacterial (outer) membrane, it is possible to separate saturation binding from the biological action of **BPI**, indicating that steps beyond surface binding are needed for the antibacterial action. Outer membrane properties were modified by reducing temperature during **BPI**-Escherichia coli interaction, growing E. coli at 42.degree. C to increase the saturated fatty acid content of membrane phospholipids, and/or using smooth E. coli with a natively less fluid outer membrane. Hydrophobic interaction chromatography on phenyl-Sepharose and measurement of sensitivity to the hydrophobic **antibiotic** rifampicin were used to monitor the changes in hydrophobic properties of the bacterial outer membrane produced by these manipulations. Nearly all **BPI** can be removed from the bacterial surface by 80 mM MgCl2 or by trypsin. At 37.degree. C, removal of **BPI** results in repair of the envelope alterations, but viability is irreversibly lost, even when Mg2+ is added after only 15 s of exposure of the bacteria to **BPI**. Under conditions of reduced outer membrane hydrophobicity, when saturation binding still occurs within 30 s, E. coli can be rescued by addition of Mg2+ after up to 5 min exposure to **BPI**, indicating retardation of postbinding steps. Evidently, after initial binding **BPI** must enter into a hydrophobic interaction with the other membrane in order to produce its antibacterial effects. These postbinding events reversibly mediate the membrane perturbations and irreversibly trigger the bactericidal action of **BPI**.

L1 33 CAP37

=> d ti 1-

L1 ANSWER 1 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI A synthetic lipopolysaccharide-binding peptide based on the neutrophil-derived protein **CAP37** prevents endotoxin-induced responses in conscious rats.

L1 ANSWER 2 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Expression and purification of recombinant **CAP37** (rCAP37), a multifunctional inflammatory mediator.

L1 ANSWER 3 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Effect of neutrophil-derived **CAP37** on monocyte-endothelial interactions.

L1 ANSWER 4 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI PhoP-PhoQ activates transcription of pmrAB, encoding a two-component regulatory system involved in Salmonella typhimurium antimicrobial peptide resistance.

L1 ANSWER 5 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Expression of **CAP37**, a novel inflammatory mediator, in Alzheimer's disease.

L1 ANSWER 6 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI **CAP37**, a neutrophil granule-derived protein stimulates protein kinase C activity in endothelial cells.

L1 ANSWER 7 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI IL-8-induced T-lymphocyte migration: Direct as well as indirect mechanisms.

L1 ANSWER 8 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Characterization of recombinant human HBP-**CAP37**-azurocidin, a pleiotropic mediator of inflammation-enhancing LPS-induced cytokine release from monocytes.

L1 ANSWER 9 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Identification of defensin-1, defensin-2, and **CAP37**, azurocidin as T-cell chemoattractant proteins released from interleukin-8-stimulated neutrophils.

L1 ANSWER 10 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI A cationic antimicrobial peptide enhances the infectivity of Coxiella burnetii.

L1 ANSWER 11 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Sperm immobilizing activity of a synthetic bioactive peptide 20-44 of 37-kDa cationic antimicrobial protein (**CAP37**) of human neutrophils.

L1 ANSWER 12 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Effect of **CAP37** on brain endothelial cell phosphatidylcholine (PC) hydrolysis.

L1 ANSWER 13 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI **CAP37**, a neutrophil-derived multifunctional inflammatory mediator.

L1 ANSWER 14 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Effect of **CAP37** on rat aorta endothelial and smooth muscle

cell chemotaxis.

L1 ANSWER 15 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Inflammatory mediator **CAP37** inhibits nitric oxide synthase activity in rat brain endothelial cells.

L1 ANSWER 16 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Expression of **CAP37** by cytokine-activated endothelial cells.

L1 ANSWER 17 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI The thermodynamic effect of **CAP37** on lipid membranes.

L1 ANSWER 18 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI **CAP37**, an inflammatory mediator that promotes both monocyte chemotaxis and leukocyte adhesion to endothelial cells.

L1 ANSWER 19 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI **CAP37**, a mediator of monocyte chemotaxis during the second wave of inflammation.

L1 ANSWER 20 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI The effect of **CAP37** on lipid membranes.

L1 ANSWER 21 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI Cerebrovascular localization of **CAP37** in Alzheimer's disease.

L1 ANSWER 22 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI **CAP37** A MULTIFUNCTIONAL HOST DEFENSE AND INFLAMMATORY PROTEIN IDENTIFICATION OF ITS CHEMOTACTIC ANTIBIOTIC AND ENDOTOXIN BINDING DOMAINS.

L1 ANSWER 23 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI BINDING OF BOVINE PANCREATIC TRYPSIN INHIBITOR TO HEPARIN BINDING PROTEIN-**CAP37**-AZUROCIDIN INTERACTION BETWEEN A KUNITZ-TYPE INHIBITOR AND A PROTEOLYTICALLY INACTIVE SERINE PROTEINASE HOMOLOGUE.

L1 ANSWER 24 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI SYNTHETIC BACTERICIDAL PEPTIDE BASED ON **CAP37** A 37-KDA HUMAN NEUTROPHIL GRANULE-ASSOCIATED CATIONIC ANTIMICROBIAL PROTEIN CHEMOTACTIC FOR MONOCYTES.

L1 ANSWER 25 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI PROTEIN KINASE C ACTIVATION IN RAT CEREBRAL ENDOTHELIAL CELLS BY **CAP37** A NEUTROPHIL GRANULE-DERIVED CATIONIC PROTEIN.

L1 ANSWER 26 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI CHARACTERIZATION OF BOVINE NEUTROPHIL ANTIBACTERIAL POLYPEPTIDES WHICH BIND TO ESCHERICHIA-COLI.

L1 ANSWER 27 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI COMPARISON OF THE EFFECTS OF METHOXYSUCCINYL-ALA-ALA-PRO-VAL-CHLOROMETHYLKETONE-INHIBITED NEUTROPHIL ELASTASE WITH THE EFFECTS OF THE NATURALLY OCCURRING MUTATIONALLY INACTIVATED HOMOLOGUE HBP ON FIBROBLASTS AND MONOCYTES IN-VITRO.

L1 ANSWER 28 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI LPS BINDING PROTEINS IN GRANULOCYTE LYSOSOMES.

L1 ANSWER 29 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI CLONING OF THE CDNA FOR THE SERINE PROTEASE HOMOLOG **CAP37** -AZUROCIDIN A MICROBICIDAL AND CHEMOTACTIC PROTEIN FROM HUMAN GRANULOCYTES.

L1 ANSWER 30 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI **CAP37** A NEUTROPHIL PMN GRANULE-DERIVED PROTEIN WITH MONOCYTE SPECIFIC CHEMOTACTIC ACTIVITY AND LIPOPOLYSACCHARIDE LPS BINDING ACTIVITY.

L1 ANSWER 31 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI AMINO ACID SEQUENCE OF **CAP37** A HUMAN NEUTROPHIL GRANULE-DERIVED ANTIBACTERIAL AND MONOCYTE-SPECIFIC CHEMOTACTIC GLYCOPROTEIN STRUCTURALLY SIMILAR TO NEUTROPHIL ELASTASE.

L1 ANSWER 32 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI THE ONTOGENY OF A 57-KD CATIONIC ANTIMICROBIAL PROTEIN OF HUMAN POLYMORPHONUCLEAR LEUKOCYTES LOCALIZATION TO A NOVEL GRANULE POPULATION.

L1 ANSWER 33 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
TI **CAP37** A HUMAN NEUTROPHIL-DERIVED CHEMOTACTIC FACTOR WITH MONOCYTE SPECIFIC ACTIVITY.

=> d bib ab 26 30 32

L1 ANSWER 26 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
AN 93:207896 BIOSIS
DN BA95:109121
TI CHARACTERIZATION OF BOVINE NEUTROPHIL ANTIBACTERIAL POLYPEPTIDES WHICH BIND TO ESCHERICHIA-COLI.
AU LITTERI L; ROMEO D
CS DEP. BIOCHEM., BIOPHYSICS, MACROMOLECULAR CHEM., UNIV. TRIESTE, 34127 TRIESTE, ITALY.
SO INFECT IMMUN 61 (3). 1993. 966-969. CODEN: INFIBR ISSN: 0019-9567
LA English
AB Bovine neutrophils contain several cationic polypeptides which exert potent microbicidal effects in vitro. To better characterize the repertoire of these polypeptides, we have incubated extracts of bovine neutrophils or neutrophil granules at pH 4 or 7 with either a smooth strain of Escherichia coli or a rough one. Only a few polypeptides interacted with the bacterial surface and were subsequently desorbed with 200 mM MgCl2, as revealed by gel electrophoresis and analysis of Western blots (imunoblots) with appropriate antibodies. Two or the main proteins appearing in Coomissie blue-stained gels molecular masses of 53 and 15 kDa and correspond to the heavy and ligt chains of myeloperoxidase. Another prevailing protein band with a molecular mass of 31 kDa was purified and shown to be 87% identical to human azurocidin/**CAP37** in its 22-amino-acid N-terminal sequence. Proteins separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and blotted to nitrocellulose did not react with an antiserum to human bactericidal/permeability-increasing protein. Conversely, immunoglubin G against Bac7 or BAc5, two members of the antimicrobial proline- and arginine-rich polypeptide family, recognized in Western blots both the inactive precursor molecules, proBac7 and proBac5, and the mature polypeptides.

L1 ANSWER 30 OF 33 BIOSIS COPYRIGHT 1997 BIOSIS
AN 92:22358 BIOSIS
DN BR42:10058
TI **CAP37** A NEUTROPHIL PMN GRANULE-DERIVED PROTEIN WITH MONOCYTE SPECIFIC CHEMOTACTIC ACTIVITY AND LIPOPOLYSACCHARIDE LPS BINDING ACTIVITY.
AU PEREIRA H A; SPITZNAGEL J K
CS DEP. MICROBIOL. IMMUNOL., EMORY UNIV. SCH. MED., ATLANTA, GA. 30322.
SO THIRD INTERNATIONAL WORKSHOP ON CYTOKINES, STRESA, ITALY, NOVEMBER 10-14, 1991. CYTOKINE 3 (5). 1991. 482. CODEN: CYTIE9 ISSN: 1043-4666

L7 ANSWER 5 OF 27 CA COPYRIGHT 1997 ACS
AN 123:166899 CA
TI New ideas about **neutrophil antimicrobial** mechanisms: Antibiotic peptides, postphagocytic **protein** processing, and cytosolic defense factors
AU Miyasaki, Kenneth T.; Bodeau, Amy L.; Shafer, William M.; Pohl, Jan; Rekha, A.; Murthy, K.; Lehrer, Robert I.
CS School Dentistry, University California, Los Angeles, CA, 90024, USA
SO Mol. Pathog. Periodontal Dis. (1994), 321-36. Editor(s): Genco, Robert. Publisher: Am. Soc. Microbiol., Washington, D. C. CODEN: 61LAA2
DT Conference; **General Review**
LA English
AB A review with 73 refs. Topics discussed include **antimicrobial** substances in human **neutrophils**; defensins; cathepsin G; and calprotectin;.
CC 15-0 (Immunochemistry)
ST review **antimicrobial** peptide **neutrophil**
IT Microbicidal and microbiostatic action
Neutrophil
(**antimicrobial** peptides in **neutrophils** in relation to microbicidal action)
IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(**antimicrobial**; **antimicrobial** peptides in **neutrophils** in relation to microbicidal action)

L7 ANSWER 8 OF 27 CA COPYRIGHT 1997 ACS
AN 122:262976 CA
TI Defensins in granules of phagocytic and non-phagocytic cells
AU Selsted, Michael E.; Ouellette, Andre J.
CS College of Medicine, University of California, Irvine, CA, 92717, USA
SO Trends Cell Biol. (1995), 5(3), 114-19 CODEN: TCBIEK; ISSN: 0962-8924
DT Journal; **General Review**
LA English
AB A review with 47 refs. **Antimicrobial proteins** stored in lysosome-like granules of **neutrophils** and macrophages probably play an important role in killing phagocytosed microbes after delivery to the phagolysosome. Among the granules' **antimicrobial** armamentarium are defensins, peptides that kill a broad spectrum of microorganisms in vitro. **Antimicrobial** defensins were recently also isolated from non-phagocytic granulocytes of the mouse small intestinal epithelium, from where they are secreted into the lumen to function extracellularly.
CC 15-0 (Immunochemistry)
ST defensin granule phagocyte nonphagocyte review
IT Macrophage
Neutrophil
(defensins in granules of phagocytic and non-phagocytic cells)
IT Organelle
(granule, defensins in granules of phagocytic and non-phagocytic cells)
IT Intestine
(small, epithelium, defensins in granules of phagocytic and

ANSWER 1 OF 4 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD

AN 93-320680 [40] WPIDS
CR 91-051334 [07]; 97-164534 [15]; 97-271364 [24]
DNC C93-142726
TI Peptide fragments of CAP37 protein - with chemotactic, **antibiotic** and lipo polysaccharide-binding activities.
DC B04 D16
IN PEREIRA, H A; SPITZNAGEL, J K
PA (UYEM-N) UNIV EMORY; (UYEM-N) UNIV EMORY SCHOOL MEDICINE
CYC 20
PI WO 9319087 A1 930930 (9340)* EN 106 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9348089 A 931021 (9407)
US 5458874 A 951017 (9547) 51 pp
US 5484885 A 960116 (9609) 50 pp
ADT WO 9319087 A1 WO 93-US2580 930319; AU 9348089 A AU 93-48089 930319; US 5458874 A CIP of US 89-375739 890705, CIP of US 90-543151 900625, Cont of US 92-855417 920319, US 92-969931 921030; US 5484885 A CIP of US 89-375739 890705, CIP of US 90-543151 900625, US 92-855417 920319
FDT AU 9348089 A Based on WO 9319087
PRAI US 92-855417 920319; US 89-375739 890705; US 90-543151 900625; US 92-969931 921030
AB WO 9319087 A UPAB: 970619
A peptide derived from the 115th to 122nd aminoacid region of CAP37, having chemotactic activity for monocytes, comprises the aminoacid sequence Ala Thr Val Glu Ala Gly Thr Arg (1).

Also claimed are: a peptide derived from the 133rd to 141st aminoacid region of CAP37 with chemotactic activity for monocytes, comprising the aminoacid sequence Ser Gly Gly Arg Leu Ser Arg Phe Pro (3) a peptide derived from the 45th to 51st aminoacid region of CAP37, with chemotactic activity for monocytes, comprising the aminoacid sequence Ser Gin Asn Pro Gly Val Ser (5) a peptide derived from the 23rd to 42nd aminoacid region of CAP37, capable of binding bacterial lipopolysaccharide, comprising the aminoacid sequence Arg His Phe Cys Gly Gly Ala Leu lle His Ala Arg Phe Val Met Thr Ala Ala Ser Cys DNA molecules encoding the various peptides and purified antibodies specifically reactive to the various peptides.

USE - The peptide fragments are derived from CAP37, which is an approx. 37,000 dalton cationic granule protein synthesised by human polymorphonuclear **leukocytes** (PMN) The peptide fragments are esp. useful for treating wounds due to their monocyte chemotactic activity and **antibiotic** or lipolysaccharide-binding activitop

Dwg.0/17

=> dhis

'DHIS' IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> d his

(FILE 'HOME' ENTERED AT 16:13:24 ON 12 AUG 1997)

32, 30,26

P'S BPI - Bactericidal Permeability Increasing protein
CAP57 *
CAP37 * BAC1 ~ BAC5

```
     FILE 'MEDLINE' ENTERED AT 16:13:36 ON 12 AUG 1997
L1        116863 S LE[redacted]OCYTE# OR LEUKOCYTE#
L2        135825 S E[redacted]HROCYTE# OR (RED BLOOD CELL#)
L3        242776 S L1 OR L2
L4        136634 S ANTIBIOTIC#
L5          3829 S BACTERIA# (5A) INHIBIT?
L6        139555 S L5 OR L4
L7          3383 S L3 AND L6
L8         13609 S DEXTOR FICOL
L9         16343 S DEXTOR FICOLL
L10           22 S L9 AND L7

     FILE 'WPIDS' ENTERED AT 16:24:17 ON 12 AUG 1997

     FILE 'MEDLINE' ENTERED AT 16:24:58 ON 12 AUG 1997
L11       13596 S DEXT
L12          17 S L7 AND L11

     FILE 'WPIDS' ENTERED AT 16:25:56 ON 12 AUG 1997
L13        6030 S L3
L14       20249 S L6
L15         108 S L13 AND L14
L16       23657 S FICOLL OR DEXTOR GRADIENT
L17           4 S L15 AND L16
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1        107304 S PD>19970801
L2        10395 S ERYTHROCYTE# OR (RED BLOOD CELLS)
L3         1015 S L1 AND L2
L4        13069 S DEXT
L5          225 S L3 AND L4
L6        26506 S ANTIBACTERIAL OR ANTIBIOTIC OR MICROBICIDAL
L7           66 S L5 AND L6
L8           70 S 424/93.71/CCLS
L9           19 S 424/93.73/CCLS
L10         210 S 424/529/CCLS
L11         119 S 424/533/CCLS
L12          94 S 424/534/CCLS
L13         420 S L8 OR L9 OR L10 OR L11 OR L12
L14          36 S L13 AND L1

=> log hold

 SESSION WILL BE HELD FOR 30 MINUTES
U.S. Patent & Trademark Office SESSION SUSPENDED AT 11:29:23 ON 08 MAY 199
8
Connection closed by remote host
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8 ANSWER 1 OF 84 MEDLINE
AN 97391404 MEDLINE
DN 97391404
TI **Erythrocyte** depletion of human umbilical cord blood using **dextran** sedimentation.
AU Tanavde V M; Desai S S; Rao S G
CS Chemo & Stem Cell Biology Division, Tata Memorial Centre, Mumbai.
SO INDIAN JOURNAL OF MEDICAL RESEARCH, (1997 Jul) 106 16-9.
Journal code: GJF. ISSN: 0971-5916.
CY India
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 199711
EW 19971104
AB We report on the results of a study using high molecular weight dextran for depletion of red blood cells (RBCs) from cord blood. Our technique achieved efficient RBC depletion by sedimentation without a significant loss in haemopoietic stem cells. Cord blood units were fractionated for erythrocyte depletion by unit gravity sedimentation in 3 per cent high molecular weight dextran. Dextran sedimentation enabled recovery of more than 80 per cent of the total nucleated cells present and 100 per cent mononuclear cell (MNC) recovery as compared to unfractionated cord blood. A four-fold increase in the colony forming unit-granulocyte macrophage (CFU-GM) number per 2 x 10(5) cells was observed after dextran treatment suggesting that this step also resulted in the enrichment of stem cells.